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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 08/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/926,001	SCHRODER ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 May 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *28 June 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see Advisory Attachment*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: *NONE*.

Claim(s) objected to: *NONE*.

Claim(s) rejected: *11-46*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☒ Other: *Advisory Attachment.*

Advisory Attachment

1. This Office Action is responsive to Applicant's amendment and response filed May 12, 2004. Claims 11-12, 16, 20, 21, 25,28, 29, 34, 38, 39 and 43 have been amended. Claims 1-10 have been cancelled. For clarification of the record, claims 30 and 33 are not new claims but claims that have been previously presented.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Rejections Maintained

3. The rejection of claims 11-16, 18-27 and 29-36 under 35 U.S.C. 103(a) as unpatentable over Youmans et al in view of Schroder is maintained for the reasons set forth on pages 3-6, paragraph 4 of the Final Office Action.

The rejection was on the grounds Youmans et al teach a tuberculosis vaccine comprising killed *Mycobacterium tuberculosis* which were killed by heat or chemicals (page 108). Youmans et al teach that the *Mycobacterium tuberculosis* was contained in phosphate buffer solution (page 109). Youmans et al teach that mice were administered the killed vaccine both with and without an adjuvant (pages 111-112).

Youmans et al do not teach adjuvants that comprise monoglycerides.

Schroder teaches the use of monoglycerides as adjuvants. Schroder teaches that the parenteral or mucosal administration of a pharmaceutical formulation containing monoglycerides (i.e. mono-olein/oleic acid) improves the immune response against admixed antigens/vaccines (page 4, lines 16-25). Schroder teaches that a combination between a monoglyceride and a fatty acid can stimulate the immune system to produce antibodies and induce protective immunity (page 7, lines 6-9). Limitations such as "mucosal administration is being view as a limitation of intended use. However, it is well known in the art that lipid preparations that are used as adjuvants are not restricted to one mode of administration and can be used in many routes of administration including

mucosal. Limitations such as packaging the vaccine as an aersol, spray or nose-drop package is being viewed as a limitation of design choice.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the monoglyceride preparation as taught by Schroder to the *Mycobacterium tuberculosis* of Youmans et al because Schroder teaches that a combination between a monoglyceride and a fatty acid can stimulate the immune system to produce antibodies and induce protective immunity (page 7, lines 6-9). It would have been expected barring evidence to the contrary, that the addition of monoglycerides to *Mycobacterium tuberculosis* vaccines would provide enhancement of immunological responses after administration of monoglycerides and/or fatty acids together with antigens and the use of monoglycerides in vaccines are stable, cheaper and easy to formulate.

Applicant urges that the claim limitation "inactivated *Mycobacterium tuberculosis* bacteria" cannot be ignored. Applicant urges that Example 1 of the instant specification clearly establishes the patentability of the claimed subject matter. Applicant urges that in Example 1, heat-killed BCG in the adjuvant formulation resulted in a positive body weight development compared to living BCG. Applicant urges that Examples 2 and 3 support these findings and further demonstrate the importance that the primary vaccination also is performed with inactivated BCG. Applicant urges that the problem to be addressed is the formulation of an improved TB vaccine. Applicant urges that Schroder suggests an adjuvant for a vaccine formulation and Schroder does not suggest a TB vaccine. Applicant urges that Youmans et al teaches a tuberculosis vaccine comprising heat or chemically killed *Mycobacterim tuberculosis*. Applicant urges that Youmans et al asserts that live mycobacterial cells are several hundred times more effective as immunizing agents against tuberculosis infection than autoclaved or inactivated cells. Applicant urges that there is no evidence that a TB vaccine comprising inactivated *Mycobacterium tuberculosis* would be effective. Applicant urges that administering the *M. tuberculosis* cells together with adjuvant does not render it

obvious to produce a TB vaccine composition as described and claimed in the present application comprising whole cell *M. tuberculosis* together with an adjuvant. Applicant urges that Schroder teaches the use of an adjuvant for stimulating the immune response but there is no mention that such an adjuvant would be suitable for use in situations where Freund's adjuvant has no effect or negative effect on the immune response.

Applicant's arguments filed May 12, 2004 have been fully considered but they are not persuasive. It is the Examiner's position that applicant argues the references individually without clearly addressing the combination of teachings. It is the combination of all of the cited and relied upon references which make up the state of the art with respect to the claimed invention. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the claims are drawn to a tuberculosis vaccine composition comprising an adjuvant one of more substances selected from the group consisting of: a) monoglyceride preparations, b) a fatty acid and c) as a immunizing component, inactivated *Mycobacterium tuberculosis* bacteria and an aerosol, spray or nose package comprising the TB vaccine. Youmans et al teach tuberculosis vaccine comprising killed

Mycobacterium tuberculosis. Youmans et al do not teach adjuvants that comprise monoglycerides. However, Schroder teaches the use of monoglycerides as adjuvants. Although "routes of administration" (i.e. nasal, pulmonary, oral or vaginal) are limitations of intended use, Schroder teaches that the parenteral or mucosal administration of a pharmaceutical formulation containing monoglycerides (i.e. mono-olein/oleic acid) improves the immune response against admixed antigens/vaccines (page 4, lines 16-25). It would be obvious to add the adjuvant comprising monoglyceride preparations and fatty acids as taught by Schroder to the tuberculosis vaccine comprising killed *Mycobacterium tuberculosis* of Youmans et al because Schroder teaches that a combination between a monoglyceride and a fatty acid can stimulate the immune system to produce antibodies and induce protective immunity. It should be remembered that claim limitations as "an aerosol, spray or nose package" are being viewed as limitations of design choice. To address Applicant's assertion that live mycobacterial cells are more effective than dead or killed mycobacterial cells, it should be noted that Youmans et al states "in spite of the evidence, the opinion is still widely held that the only difference in the immunizing capacity of dead and living attenuated mycobacterial cell is quantitative" (page 108). Youmans et al further teach that other parameters such as the age of cells used to immunize, time of challenge, route of challenge, method of killing cells and effective adjuvants need to be measured more validly (page 108). In regards to the examples in the instant specification, Example 1, adds support to the position that heat-killed mycrobacterial cells are more effective in immunizing mice than live mycobacterial cells. Examples 2 and 3 of the instant specification supports the

position that inactivated (heat-killed) cells are superior over live cells in regards to immunization against *Mycobacterium tuberculosis* infections. It is the Examiner's position that there is nothing on the record to teach or suggest that the combination of references do not teach the claimed invention.

4. The rejection of claims 38-45 under 35 U.S.C. 103(a) as unpatentable over Youmans et al in view of Schroder is maintained for the reasons set forth on pages 6-8 paragraph 5 of the previous Office Action.

The rejection was on the grounds that Youmans et al teach a method of vaccinating mice comprising administering killed *Mycobacterium tuberculosis* with and without Freund's adjuvant (pages 111-112). Youmans et al teach that administration of the tuberculosis vaccine did indeed provoke immune response (page 110).

Youmans et al do no teach the use of monoglycerides as adjuvants.

Schroder teaches a method of vaccinating mice comprising a diphtheria antigen and a monoglyceride preparation (page 9, example 4). Schroder teaches that both IgG as well as protective antibody titers were at the same level as compared to the control groups which received a composition of diptheria toxoid and alum. Schroder also teaches that the high IgG titers always were accompanied by high neutralization titers indicating that the formulations do no destroy the antigenic sites that are important for protective immunity (page 9, Example 4).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the to monoglyceride preparation of Schroder to the *Mycobacterium tuberculosis* vaccine composition used in the method of vaccinating a mammal as taught by Youmans et al because Schroder teaches that the parenteral or mucosal administration of a pharmaceutical formulation containing monoglycerides (i.e. mono-olein/oleic acid) improves the immune response against admixed antigens/vaccines (page 4, lines 16-25). It would have been expected barring evidence to the contrary, that the addition of monoglycerides to *Mycobacterium tuberculosis* vaccines would provide enhanced immunogenicity of antigens and that formulations are stable, inexpensive and easy to formulate.

Applicant urges that claims 38-45 under 35 U.S.C. 103(a) as unpatentable over Youmans et al in view of Schroder is traversed for the reason as set forth above.

Applicant urges that Youmans et al do not teach the use of adjuvants as beneficial and furthermore the method using inactivated *M. tuberculosis* cells provide poor results. Applicant urges that one skilled in the art would consider the Youman et al teaching away from the claimed invention and would not be an expectation of success.

Applicant's arguments filed May 12, 2004 have been fully considered but they are not persuasive. It is the Examiner's position that applicant argues the references individually without clearly addressing the combination of teachings. It is the combination of all of the cited and relied upon references, which make up the state of the art with respect to the claimed invention. The claims are drawn to a method of vaccinating a mammal against TB which comprises mucosal administration to the mammal of a protection-inducing amount of a tuberculosis vaccine composition comprising an adjuvant one of more substances selected from the group consisting of: a) monoglyceride preparations, b) a fatty acid and c) as a immunizing component, inactivated *Mycobacterium tuberculosis* bacteria. Youmans et al a method of vaccinating mice comprising administering killed *Mycobacterium tuberculosis* with and without Freund's adjuvant (pages 111-112). Youmans et al do not teach the use of monoglycerides as adjuvants. However, Schroder teaches the use of monoglycerides as adjuvants. Although "routes of administration" (i.e. nasal, pulmonary, oral or vaginal) are limitations of intended use, Schroder teaches that the parenteral or mucosal administration of a pharmaceutical formulation containing monoglycerides (i.e. mono-olein/oleic acid) improves the immune response against admixed antigens/vaccines (page 4, lines 16-25). It would be obvious to add the adjuvant comprising

monoglyceride preparations and fatty acids as taught by Schroder to the tuberculosis vaccine comprising killed *Mycobacterium tuberculosis* of Youmans et al because Schroder teaches that a combination between a monoglyceride and a fatty acid can stimulate the immune system to produce antibodies and induce protective immunity. In regards to Applicant's arguments concerning that the method would not be an effective method of vaccinating mammals, it should be noted that Youmans et al teach that administration of the tuberculosis vaccine did indeed provoke immune response and Schroder teaches that the parenteral or mucosal administration of a pharmaceutical formulation containing monoglycerides (i.e. mono-olein/oleic acid) improves the immune response against admixed antigens/vaccines. Additionally, Youmans et al states "in spite of the evidence, the opinion is still widely held that the only difference in the immunizing capacity of dead and living attenuated mycobacterial cell is quantitative" (page 108). Youmans et al further teach that other parameters such as the age of cells used to immunize, time of challenge, route of challenge, method of killing cells and effective adjuvants need to be measured more validly (page 108). It should be remembered that Example 1, adds support to the position that heat-killed mycrobacterial cells are more effective in immunizing mice (i.e. body weight gain) than live mycobacterial cells. Examples 2 and 3 of the instant specification supports the position that inactivated (heat-killed) cells are superior over live cells in regards to immunization against *Mycobacterium tuberculosis* infections. In regards to Applicant's comment concerning "obvious to try", Youmans et al teaches vaccine compositions that comprise adjuvants that have been successful at immunizing animals against infection.

Schroder has demonstrated that the adjuvant of his invention has been used to enhance the response of an antigen towards an immune response. Therefore, there is an expectation of success when the teachings of the prior art references are combined. It is the Examiner's position that there is nothing on the record to teach or suggest that the combination of references do not teach the claimed invention.

5. The rejection claims 11-37 under 35 U.S.C. 103(a) as unpatentable over Youmans et al, Schroder and Van Nest et al is maintained for the reasons set forth on pages 9-11, paragraph 7 of the Final Office Action.

The rejection was on the grounds that Youmans et al teach a tuberculosis vaccine comprising killed *Mycobacterium tuberculosis* which were killed by heat or chemicals (page 108). Youmans et al teach that the *Mycobacterium tuberculosis* were contained in phosphate buffer solution (page 109). Youmans et al teach that mice were administered the killed vaccine both with and without an adjuvant (pages 111-112).

Youmans et al do not teach adjuvants that comprise monoglycerides.

Schroder teaches the use of monoglycerides as adjuvants. Schroder teaches that the parenteral or mucosal administration of a pharmaceutical formulation containing monoglycerides (i.e. mono-olein/oleic acid) improves the immune response against admixed antigens/vaccines (page 4, lines 16-25). Schroder teaches that a combination between a monoglyceride and a fatty acid can stimulate the immune system to produce antibodies and induce protective immunity (page 7, lines 6-9). Limitations such as "mucosal administration is being view as a limitation of intended use. However, it is well known in the art that lipid preparations that are used as adjuvants are not restricted to one mode of administration and can be used in many routes of administration including mucosal. Limitations such as packaging the vaccine as an aersol, spray or nose-drop package is being viewed as a limitation of design choice.

Youmans et al and Schroder do not teach soybean oil.

Van Nest et al teach the use of any metabolizable oil (for example, soybean oil) in an adjuvant formulation (column 3, lines 62-67 – column 4, lines 1-11). Van Nest et al teach that the oil component of the adjuvant can be present in an amount from 0.5% to 20% by volume (column 4, lines 49-53). Van Nest et al teach that metabolizable oils such as soybean oil are used in vaccines because unmetabolizable oils when administered may cause abscesses, granulomas or even carcinomas and meat of birds and animals vaccinated with oil other than metabolizable oils may be unacceptable for

human consumption due to the deleterious effect that unmetabolizable oils have on the consumer (column 3, lines 62-67 and column 4, lines 1-3).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the monoglyceride preparation as taught by Schroder to the *Mycobacterium tuberculosis* of Youmans et al and the soybean oil as taught by Van Nest et al because Schroder teaches that a combination between a monoglyceride and a fatty acid can stimulate the immune system to produce antibodies and induce protective immunity (page 7, lines 6-9) and Van Nest et al teach that metabolizable oils such as soybean oil are used in vaccines because unmetabolizable oils when administered may cause abscesses, granulomas or even carcinomas and meat of birds and animals vaccinated with oil other than metabolizable oils may be unacceptable for human consumption due to the deleterious effect that unmetabolizable oils have on the consumer (column 3, lines 62-67 and column 4, lines 1-3). It would have been expected barring evidence to the contrary, that the addition of an adjuvant comprising monoglycerides and soybean oil to *Mycobacterium tuberculosis* vaccines would provide enhancement of immunological responses to the *Mycobacterium tuberculosis* antigen.

Applicant urges that as discussed above, Applicants do not believe that a *prima facie* case of obviousness has been established. Applicant urges that the combination of Youmans et al, Schroder and Van Nest et al do not teach the claimed invention. Applicant urges that there is no motivation to combine the teachings of the prior art. Applicant urges that there is no indication in Van Nest et al that a metabolizable oil used in an adjuvant can be suitable for mucosal administration.

Applicant's arguments filed May 12, 2004 have been fully considered but they are not persuasive. It is the Examiner's position that applicant argues the references individually without clearly addressing the combination of teachings. It is the combination of all of the cited and relied upon references, which make up the state of the art with respect to the claimed invention. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the

prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Youmans et al teach a tuberculosis vaccine comprising killed *Mycobacterium tuberculosis*. Youmans et al do not teach adjuvants that comprise monoglycerides. However, Schroder teaches the use of monoglycerides as adjuvants. Although "routes of administration" (i.e. nasal, pulmonary, oral or vaginal) are limitations of intended use, Schroder teaches that the parenteral or mucosal administration of a pharmaceutical formulation containing monoglycerides (i.e. mono-olein/oleic acid) improves the immune response against admixed antigens/vaccines (page 4, lines 16-25). Youmans et al and Schroder do not teach the use of a metabolizable oil. Van Nest et al teach that Van Nest et al teach the use of any metabolizable oil (for example, soybean oil) in an adjuvant formulation. Van Nest et al teach that metabolizable oils such as soybean oil are used in vaccines because unmetabolizable oils when administered may cause abscesses, granulomas or even carcinomas. It would be obvious to add the metabolizable oil (i.e. soybean oil) as taught by Van Nest to the vaccine composition of Youmans et al and Schroder combined because Van Nest has demonstrated the use of metabolizable oils in adjuvant formulations. One of skill in the art would be motivated to add metabolizable oils to vaccine compositions because Van Nest teach that metabolizable oils should be added to vaccine formulations because unmetabolizable oils when administered may cause abscesses, granulomas or even

carcinomas and meat of birds and animals vaccinated with oil other than metabolizable oils may be unacceptable for human consumption due to the deleterious effect that unmetabolizable oils have on the consumer.

6. The rejection claims 38-46 under 35 U.S.C. 103(a) as unpatentable over Youmans et al, Schroder and Van Nest et al is maintained for the reasons set forth on pages 12-13, paragraph 8 of the Final Office Action.

The rejection was on the grounds that Youmans et al teach a method of vaccinating mice comprising administering killed *Mycobacterium tuberculosis* with and without Freund's adjuvant (pages 111-112). Youmans et al teach that administration of the tuberculosis vaccine did indeed provoke immune response (page 110).

Youmans et al do no teach the use of monoglycerides as adjuvants.

Schroder teaches a method of vaccinating mice comprising a diphtheria antigen and a monoglyceride preparation (page 9, example 4). Schroder teaches that both IgG as well as protective antibody titers were at the same level as compared to the control groups which received a composition of diptheria toxoid and alum. Schroder also teaches that the high IgG titers always were accompanied by high neutralization titers indicating that the formulations do no destroy the antigenic sites that are important for protective immunity (page 9, Example 4).

Youmans et al and Schroder do not teach soybean oil.

Van Nest et al teach the use of any metabolizable oil (for example, soybean oil) in an adjuvant formulation (column 3, lines 62-67 – column 4, lines 1-11). Van Nest et al teach that the oil component of the adjuvant can be present in an amount from 0.5% to 20% by volume (column 4, lines 49-53). Van Nest et al teach that metabolizable oils such as soybean oil are used in vaccines because unmetabolizable oils when administered may cause abscesses, granulomas or even carcinomas and meat of birds and animals vaccinated with oil other than metabolizable oils may be unacceptable for human consumption due to the deleterious effect that unmetabolizable oils have on the consumer (column 3, lines 62-67 and column 4, lines 1-3).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the monoglyceride preparation as taught by Schroder to the *Mycobacterium tuberculosis* of Youmans et al and the soybean oil as taught by Van Nest et al use in a method of vaccinating a mammal because Schroder teaches that a combination between a monoglyceride and a fatty acid can stimulate the immune system to produce antibodies and induce protective immunity (page 7, lines 6-9) and Van Nest et al teach that metabolizable oils such as soybean oil are used in vaccines because unmetabolizable oils when administered may cause abscesses,

granulomas or even carcinomas and meat of birds and animals vaccinated with oil other than metabolizable oils may be unacceptable for human consumption due to the deleterious effect that unmetabolizable oils have on the consumer (column 3, lines 62-67 and column 4, lines 1-3). It would have been expected barring evidence to the contrary, that the addition of an adjuvant comprising monoglycerides and soybean oil to *Mycobacterium tuberculosis* vaccines would provide enhancement of immunological responses to the *Mycobacterium tuberculosis* antigen.

Applicant did not address this rejection in the submitted response.

This rejection is maintained for the reasons of record as set forth on pages 12-13 of the Final Office action.

Conclusion

7. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
August 1, 2004

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